

Specification (marked-up version showing amendments)

Page 1, line 1:

Process for Preparation of MR Contrast Agents

Page 1, line 3, insertion of:

This application is a continuation application of international application number PCT/GB00/01897 filed May 17, 2000, the entire disclosure of which is hereby incorporated by reference.

Background of Invention

Page 2, line 33, insertion of:

While WO99/24080 does describe means by which para-hydrogen hydrogenation may be effected, we have now found that hydrogenation to harness for MRI the p-H₂ and/or o-D₂ induced hyperpolarization, the hydrogenation reaction is particularly favourably performed by mixing gaseous para-hydrogen and/or ortho-deuterium enriched hydrogen (i.e. where the p:o ratio of ¹H₂ is greater than 1:3, particularly greater than 3:7, more particularly greater than 1:1 and/or the o:p ratio of ²H₂ is greater than 3:2, particularly greater than 3:1, more particularly greater than 4:1) with a spray of a solution of the unsaturated compound and a hydrogenation catalyst.

Summary of Invention

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Page 3, lines 17-27, deletion of:

[While WO99/24080 does describe means by which para-hydrogen hydrogenation may be effected, we have now found that hydrogenation to harness for MRI the p-H₂ and/or o-D₂ induced hyperpolarization, the hydrogenation reaction is particularly favourably performed by mixing gaseous para-hydrogen and/or ortho-deuterium enriched hydrogen (i.e. where the p:o ratio of ¹H₂ is greater than 1:3, particularly greater than 3:7, more particularly greater than 1:1 and/or the o:p ratio of ²H₂ is greater than 3:2, particularly greater than 3:1, more particularly greater than 4:1) with a spray of a solution of the unsaturated compound and a hydrogenation catalyst.]

Page 5, line 35, insertion of:

Brief Description of the Figures

Figure 1 is a schematic view of one apparatus according to the invention;

Figure 2 is a schematic view of part of the apparatus of Figure 1;

Figure 3 is a schematic view of a further part of the apparatus of Figure 1; and

Figure 4 is a schematic view of a further aspect of the present invention.

Detailed Description of the Invention

Page 13, lines 8-19, deletion of:

[Embodiments of the process and apparatus of the invention will now be described with reference to the following non-limiting Example and to the accompanying drawings, in which:



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Claims (marked-up version showing amendment(s))

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[Claims]

What is claimed is:

1. (once amended) A process for the preparation of an MR contrast agent[, said process] comprising:
 - i) obtaining a solution in a solvent of a hydrogenatable, unsaturated substrate compound and a catalyst for the hydrogenation of said substrate compound;
and
 - ii) introducing said solution in droplet form into a chamber containing hydrogen gas (H_2) enriched in para-hydrogen ($p\text{-}^1H_2$) and/or ortho-deuterium ($o\text{-}^2H_2$)
[whereby]to hydrogenate said substrate to form a hydrogenated imaging agent[;
 - iii) optionally subjecting said hydrogenated imaging agent to a magnetic field having a field strength below earth's ambient field strength;
 - iv) optionally dissolving said imaging agent in an aqueous medium;
 - v) optionally separating said catalyst from the solution of said imaging agent in said aqueous medium;
 - vi) optionally separating said solvent from the solution of said imaging agent in said aqueous medium; and

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vii)optionally freezing the solution of said imaging agent in said aqueous medium].

2. (once amended) [A]The process [as claimed in claim 1]of claim 14 wherein said field strength in step (iii) is less than 50 μ T.
3. (once amended) [A]The process [as claimed in claim 1]of claim 14 wherein said field strength in step (iii) is less than 1 μ T.
4. (once amended) [A]The process [as claimed in claim 1]of claim 14 wherein said field strength in step (iii) is less than or equal to 0.1 μ T.
5. (once amended) [A]The process [as claimed in claim 1]of claim 14 wherein said field strength in step (iii) is cycled in a first part from earth's ambient field strength to a field strength less than 0.1 μ T, [then]and in a second part back to ambient field strength again.
6. (once amended) [A]The process [as claimed in]of claim 5 wherein the first part of the cycle is [of the order of]approximately ≤ 1 ms and the second part is [of the order of]approximately 10-10000 ms.

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7. (once amended) [A]The process [as claimed in any one of the preceding claims]of claim 1 wherein said process is carried out directly in water and wherein both said substrate and said catalyst are water-soluble.
 9. (once amended) [An]The apparatus [as claimed in]of claim 8 wherein said hydrogenation apparatus is further provided with magnetic shielding such that the magnetic field within at least part of said hydrogenation chamber and/or within at least part of said conduit is $<50 \mu\text{T}$.
 10. (once amended) [An]The apparatus [as claimed in]of claim 9 wherein said magnetic field is $<1 \mu\text{T}$.
 11. (once amended) [An]The apparatus [as claimed in]of claim 9 wherein said magnetic field is $<0.1 \mu\text{T}$.
 12. (once amended) [An]The apparatus [as claimed in any one of claims 8 to 11]of claim 8 wherein said conduit is provided with a liquid inlet between said hydrogenation chamber and said catalyst removal chamber.
 14. (new) The process of claim 1 further comprising subjecting said hydrogenated imaging agent to a magnetic field having a field strength at or below the ambient magnetic field strength of the earth.

15. (new) The process of claim 1 further comprising dissolving said imaging agent in an aqueous medium.
16. (new) The process of claim 14 further comprising separating said catalyst from said solution of imaging agent in aqueous medium.
17. (new) The process of claim 14 further comprising separating said solvent from said solution of imaging agent in aqueous medium.
18. (new) The process of claim 14 further comprising freezing solution of imaging agent in aqueous medium.

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